Newsletter of the VA Special Interest Group of the Consortium of MS Centers

VASIGNATURE

Volume 6, Number 1, Spring 2007

Welcome to Our Latest Edition

Our goal is to provide a medium for VA MS professionals to share expertise and improve care for MS patients. We welcome your thoughts, comments, and participation.
Please pass this issue along. If you know someone who wishes to be included on the electronic distribution list, forward the email address to the editor.

A Letter from the Editor

Welcome to the latest edition of the *VASIGnature*. We have changed our usual format this issue to allow space for an article on MRI in Multiple Sclerosis by Dr. Edward Daly. In addition, instead of the usual literature review we have included for you an extensive bibliography to accompany the text that is separated into topics to make finding further information easier. We hope you find this change in format useful. Please let us know what you think of the new format as well as topics you would like to see in future issues.

We would also like to take this opportunity to remind you of the upcoming Consortium of Multiple Sclerosis Centers Annual Meeting in Washington, DC. Information is available on the website www.mscare.org along with a program. The Department of Veterans Affairs (VA) will be well represented with a large thank you to the continued financial support of the Paralyzed Veterans of America and United Spinal Association.

Finally, as always, feel free to pass this newsletter on. If you know of someone who is not getting a copy, please have them email me directly. We welcome your ideas and suggestions for future issues. The next issue will be Summer 2007, and as we have done before, we plan to publish the list of VA speakers and their talks along with notes from the consortium meeting.

I hope to see you in Washington.

Sincerely,

Deborah Downey, ANP
Editor
deborah.downey@va.gov

In this Issue:

In this issue we continue the series of articles to help clinicians diagnose and treat MS.

MRI in MS

by Edward Daly, MD, PhD

Over the past 25 years MRI has become the most important ancillary tool in the diagnosis and management of patients with multiple sclerosis. From the initial ambiguity of UBOs (Unidentified Bright Objects), technology, research, and clinical experience with MRI have evolved not only to the point where MRI imaging is nearly essential clinically but also has driven a better understanding of the pathophysiology of multiple sclerosis. However, limited specificity accompanies the exquisite sensitivity of MRI—multiple sclerosis remains a clinical diagnosis. The MRI is used in MS to support the clinical diagnosis and to exclude other disorders with similar clinical presentations. Perhaps the two most exciting aspects of neuroimaging are the visualization of "clinically silent" lesions and the potential for monitoring response to therapeutic interventions. This latter aspect is driven by relatively rapid reduction in MRI lesions seen with the introduction of DMT. Excellent reviews discussing the scope and details of clinical MRI imaging in MS, as well as research methodologies, are available. [1–4]

Conventional MRI imaging uses a combination of T1-weighted, T2-weighted, and gadiolinium enhancement techniques and is widely available. FLAIR (fluid-attenuated inversion-recovery) sequences are especially valuable in cerebral imaging. The Consortium of MS Centers (CMSC) sponsored a consensus process for the development of a minimum standard for brain MRI imaging in MS as shown in chart 1 (1T or greater magnet; see reference 12 for parameters).

Although of limited specificity, there are findings on MRI that are characteristic of MS. T2 lesions are found widely in cerebral white matter, tend to be ovoid, and are usually greater than 5mm in size. Lesions are frequently found perpendicular to the lateral ventricles (Dawson's fingers), in the corpus callosum adjacent to the ventricles, in juxtacortical regions, in the brainstem and cerebellum, and much less commonly in the gray matter of the cerebral cortex. FLAIR sequences best demonstrate periventricular and juxtacortical lesions. The expanse of T2 lesions is often used as a surrogate of disease burden. The anatomical detail of T1 sequences best demonstrates "black holes" and atrophy, the two findings that best correlate with clinical measures of disability in both cognitive and physical domains. It should be noted that hyodensities seen on the T1 scans may be transient and that only chronic (> 3–6 months hypodensities, "black holes") correlate with disability. Gadolinium enhancing lesions on T1 imaging, more common in relapsing-remitting MS, often predict relapses and are used as a surrogate for disease activity. Enhancement is transient and resolves in several weeks (usually 2–6 weeks). Nonenhancing lesions together with lesions in various phases of enhancement provide some evidence for a dynamic pathophysiological process as opposed to a static or monophasic CNS insult. However, enhancing lesions are poor predictors of progressive disability.

Although technically more difficult than brain MRI, spinal MRI can be a valuable addition to the evaluation of MS patients. Spinal lesions in MS tend to be less than two vertebral segments in length and do not involve the entire cross-section on axial views. Such lesions, frequently asymptomatic, are found in

CHART 1

Sequence	Diagnostic Scan for Cinically Isolated Syndrome	MS Baseline or F/U Scan
3 plane (or other) scout	Recommended	Recommended
Axial FSE PD*/T2	Recommended	Recommended
Axial Fast FLAIR	Recommended	Recommended
Sagittal Fast FLAIR	Recommended	Optional
Axial pregadoliniium T1	Optional	Optional
3 D T1	Optional	Optional
Axial gadolinium enhanced T1	Recommended	Optional

*FSE PD = fast spin echo proton density

50 percent to 90 percent of MS patients. The presence or absence of spinal lesions can be especially helpful in older patients in whom small vessel ischemic disease frequently complicates the interpretation of brain MRI since ischemic disease is rare in the spinal cord. Spinal MRI (usually cervical and thoracic) should be obtained if presenting symptoms or signs suggest a cord level or if the brain MRI is equivocal in answering the diagnostic or management question. The CMSC panel has also recommended minimum standards for MRI imaging of the spinal cord in MS as shown in chart 2 (see reference 12 for parameters).

In addition to the these findings that are suggestive of MS plagues, Charil and colleagues [10] have recently published an excellent consensus statement on MRI "red flags" that should suggest consideration of other pathological processes. MRI imaging's excellent sensitivity but poor specificity increases the likelihood of false positive diagnoses of MS, especially if only nonspecific white matter lesions, and not the entire clinical presentation, are considered. "Red flags" discussed addressed include diffuse and symmetric white matter lesions; predominance of punctuate lesions; predominance of large lesions, especially large brainstem lesions; predominance of juxtcortical lesions; predominance of gray matter lesions; absence of periventricular or callosal lesions; absence of Dawson's fingers; lesions of the temporal poles, insula, or external capsule; hemorrhagic lesions; monophasic stage of enhancement of all lesions; isolated lesions with ring enhancement; prominent mass effect with lesions; infiltrative lesions that do not respect gray-white boundaries; hydrocephalus, meningeal enhancement; and prominent spinal cord swelling or presence of lesions extending more than 3 vertebral segments or involving most of the cross section of the cord.

In 2001the International Panel on the Diagnosis of MS published a consensus statement on the use of paraclinical (MRI, CSF analysis, and visual evoked potentials) evidence in MS diagnosis. These recommendations have become known as the McDonald criteria. [8] The purpose of these criteria was to facilitate, not replace, the diagnosis of MS before "dissemination in time and space" became clinically apparent. They proposed that the MRI could be used to satisfy dissemination in space and space as shown in chart 3.

Without detail it was proposed that one spinal lesion could be substituted for one brain lesion. It should be noted that a diagnosis could not be made regardless of the number of lesions on a MRI done within three months on the initial attack.

Shortly thereafter the American Academy of Neurology proposed less conservative guidelines [9] with the hope that early intervention with DMTs after an initial attack suggestive of MS (clinically isolated syndrome, CIS) might delay the progression to clinically definite MS (CDMS). After exclusion of other possible explanations for the clinical presentation (listed in the report), the guidelines proposed that the following findings were sensitive predictors (> 80 percent) for the development of CDMS within 10 years of the CIS:

- Three or more T2 white matter lesions on MRI at the time of the initial attack
- Two or more gadolinium enhancing lesions on MRI at the time of the initial attack
- New T2 lesions or gadolinium enhancement three or more months after the initial MRI

CHART 2

Sequence	Recommendation	Sequence	Recommendation
3 plane (or other) scout	Recommended	3 plane (or other scout)	Recommended
Postcontrast sagittal FSE PD/T2	Recommended	Precontrast sagittal FSE PD/T2	Recommended
Postcontrast axial FSE PD/T2	Through suspicous lesions	Precontrast axial FSE PD/T2	Through suspicious lesions
Postcontrast sagittal T1	Recommended	Postcontrast sagittal T1	Recommended
Postcontrast axial T1	Through suspicous lesions	Postcontrast-enhanced axial T1	Through suspicious lesion(s)
Postcontrast 3D T1	Optional	3D T1	Optional

CHART 3

Dissemination in Space (3 of 4) satisfied	Dissemination in Time
one grade-enhancing lesion of nine T2 lesions	A gado-enhancing lesion at a second site on an MRI done more than 3 months after the initial attack
one or more infratetentorial lesions	
one or more juxtcortical lesions	
three or more periventricular lesions	

No guideline or algorithm exits for systematic exclusion of "better explanations" exist—it will depend on clinical suspicion and experience.

The clinical interest and research data fostered by the original McDonald criteria led to their revision in 2005. [10] Although the International Panel remained hesitant to decrease the stringent MRI criteria for dissemination in space, the criteria for dissemination in time were relaxed to include either a gadolinium enhancing lesion at a second site at three months or the presence of a new T2 lesion compared to the initial MRI at least one month after the initial attack. Recent reports suggest less stringent criteria appear to increase sensitivity in identifying those who will progress to CDMS without sacrificing specificity in patients with typical CIS. However, estimates of both sensitivity and specificity vary widely [13,14]

It is clear that use of MRI paraclinical evidence increases both the sensitivity (50–70 percent) and specificity (70–90 percent) of the diagnosis of CDMS. However, its clinical usefulness to "rule-in" or "rule-out" a disease with such a widely varying clinical course treated with expensive pharmaceuticals, with significant side effects and relatively modest benefits, remains controversial. [15–18]

Many questions remain for the role of MRI in the clinical management of patients with MS. Can better criteria lead to even greater accuracy in the early diagnosis of MS? Can the MRI help us decide who needs early and / or more aggressive treatment? Can MRI be used to predict the clinical course the disease will take? Can routine follow-up MRI add value to the management of patients with MS (a costly paradigm frequently practiced, but discouraged by guidelines [12])? Can MRI response lead to individualization of DMT dosing so as to maximize benefit and minimize side effects? Can MRI help identify treatment failures so that alternative therapies can be instituted early? Does a stable clinical course and a quiescent MRI predict in whom lifelong therapy is not needed (i.e., can the MRI help identify a remission)?

Review

1. Bakshi R, Hutton G.J., Miller J.R., Radue E.W. The use of magnetic resonance imaging in the diagnosis and long-term management of multiple sclerosis. *Neurology* 2004; 63(Suppl 5):S3-11.

2 Napoli SQ, Bakshi R. Magnetic resonance imaging in multiple sclerosis. *Reviews in Neurological Diseases* 2005; 2:109-116.

3. Simon J.H. MRI in multiple sclerosis. *Physical Medicine & Rehabilitation Clinics of North America* 2005; 16:383–409.

4. Traboulsee A., Zhao G., Li D.K. Neuroimaging in multiple sclerosis. *Neurologic Clinics* 2005; 23:131–148.

Spinal imaging

5. Lycklama G., Thompson A., Filippi M., et al. Spinal-cord MRI in multiple sclerosis. *Lancet Neurology* 2003; 2:555–562.

6. Bot J.C., Barkhof F., Polman C.H., et al. Spinal cord abnormalities in recently diagnosed MS patients: added value of spinal MRI examination. *Neurology* 2004; 62:226–233.

7. Nielsen J.M., Barkhof F., van O., Polman C.H. The role of spinal cord imaging in the diagnosis of multiple sclerosis. *Nature Clinical Practice Neurology* 2006; 2:283–286.

Guidelines

8. McDonald W.I., Compston A., Edan G., et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Annals of Neurology* 2001; 50:121–127.

9.Frohman E.M., Goodin D.S., Calabresi P.A., et al. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2003; 61:602–611.

10. Polman C.H., Reingold S.C., Edan G., et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria." *Annals of Neurology* 2005; 58:840–846

11. Charil A., Yousry T.A., Rovaris M., et al. MRI and the diagnosis of multiple sclerosis: expanding the concept of "no better explanation." *Lancet Neurology* 2006; 5:841–852.

12. Simon J.H., Li D., Traboulsee A., et al. Standardized MR imaging protocol for multiple sclerosis: Consortium of MS Centers consensus guidelines. *American Journal of Neuroradiology* 2006; 27:455–461.

13. Swanton J.K., Fernando K., Dalton C.M., et al. Modification of MRI criteria for multiple sclerosis in patients with clinically isolated syndromes. *Journal of Neurology, Neurosurgery & Psychiatry* 2006; 77:830–833.

14. Korteweg T., Tintore M., Uitdehaag B., et al. MRI criteria for dissemination in space in patients with clinically isolated syndromes: a multicentre follow-up study. *Lancet Neurology* 2006; 5:221–227.

Opposing Viewpoints

15. Goodin D.S., Frohman E.M. Overdiagnosis of multiple sclerosis by magnetic resonance imaging. *Annals of Neurology* 2006; 59: 575–576.
16. Nielsen J.M., Korteweg T., Barkhof F., Uitdehaag B.M., Polman C.H. Overdiagnosis of multiple sclerosis and magnetic resonance imaging criteria. *Annals of Neurology* 2005; 58:781–783.
17. Poser C.M. Revisions to the 2001 McDonald diagnostic criteria. *Annals of Neurology* 2006; 59:727–728.
18. Whiting P., Harbord R., Main C., et al. Accuracy of magnetic resonance imaging for the diagnosis of multiple sclerosis: systematic review. *BMJ* 2006; 332:875–884.

EDUCATIONAL OFFERINGS

Monthly Conference Calls for CME Accreditation

The MS Centers of Excellence will have the following education calls at call number (800) 767-1750, access code 43157.

DATES

MAY 8 & 9, 4:00-5:00 PM EST

Speaker— Walter Royal, MD
Topic – "Pros and Cons of Vaccination for Patients with MS"

MAY 16 & 17, NOON-1:00 PM EST

Speaker—Deborah Downey, RN, ANP
Topic—"Complimentary and Alternative Medicine"

The Department of Veterans Affairs Medical Center is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. The VAMHCS designates this educational activity for 0.75 contact hours in continuing nursing education.

MAY 14, 8:00-9:00 PM EST

Speaker—Jacqueline Friedman, MD
Topic—TBD

JUNE 11, 8:00-9:00 PM EST

Speaker—Lynne Hammel, MS, CRNP
"Coping with Depression"

CEU

1 hour CME and CEU Credit Available

EES—The Department of Veterans Affairs Employee Edu-cation System is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The Department of Veterans Affairs Employee Education System also is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Com-mission on Accreditation. The Department of Veterans Affairs Employee Education System is approved by the American Psy-chological Association to offer continuing education for psychologists.